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Article type : Letter to the Editor

Kidney transplantation during the COVID-19 pandemic: Potential long-term consequences of an early post-transplant infection.

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Running title: Kidney transplantation during the COVID-19 pandemic

Disclosure: none

Funding: none

Keywords: COVID-19, safety, living-donor kidney transplantation, nosocomial transmission, organ transplantation

To the Editor,

Recently, Akalin et al.[1] reported a 28% mortality among kidney-transplant patients infected with Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Two of the 10 patients who died had been transplanted within the previous 5 weeks. During the coronavirus disease (COVID)-19 outbreak, kidney transplant programs were suspended in several countries[2]. Although the pandemic is still ongoing, the stop of lockdown has prompted several transplant centers to restart kidney transplantation programs. It is recommended to consider that donors and recipients are screened for SARS-CoV-2 before transplantation by means of nuclear acid tests with or without chest CT scans. Nevertheless, during the incubation period, COVID-19 may be undetectable and chest CT scan is usually normal. In addition, severe COVID-19 cases were observed early after transplantation, requiring an Intensive Care Unit (ICU) stay and a decrease in immunosuppression, which may lead to death or to a harmful impact on the kidney allograft function[1,3,4]. This was the case of a 30-year-old man who had undergone a pre-emptive ABO-compatible HLA-compatible living-donor kidney transplantation for malformative uropathy in our center on 02/26/2020, i.e. 16 days before the kidney transplant program was suspended and 20 days before lockdown began. He was given tacrolimus, mycophenolic acid and steroids without induction therapy. At discharge (day 16 post-transplantation), eGFR was 47mL/min/1.73m² (Fig.1A). At day 24, post-transplantation, he was admitted for fever (39°C), caught, shortness of breath, and diarrhea. The eGFR value was 40 mL/min/1.73m². An oropharyngeal swab specimen was obtained, which detected SARS-CoV-2. A chest CT scan showed multiple patchy ground-glass opacities in both lungs. He was given hydroxychloroquine and azithromycin upon admission for seven days. The day after, he presented with acute respiratory distress that required mechanical ventilation and developed acute kidney injury. As suggested[4], due to the severity of the disease, mycophenolic acid and tacrolimus were suspended (for 24 and 15 days, respectively). Nonetheless, due to drug-to-drug interaction (mainly with azithromycin), tacrolimus remained detectable during the whole hospitalization, and the tacrolimus trough level dropped below 5 ng/mL for fewer than 8 days.

The patient was discharged from the ICU 20 days after admission. At day 58 post-transplantation, kidney function was still impaired (eGFR at 36 mL/min/1.73m^2) and a *de novo* anti-DQ5 donor specific antibody (DSA) was detected. A kidney biopsy showed diffuse proximal tubule injury with the loss of brush border suggesting a recently described SARS-CoV-2 kidney injury,[5] associated with a borderline rejection (Fig.1B). No additional treatment was initiated, given the precariousness of the patient's respiratory state and the deterioration visible in the CT scan. At three months post-transplantation (38 days post *de novo* DSA detection), the kidney function was impaired but stable (eGFR 35 mL/min/1.73m²). In the present case, it is unknown whether the occurrence of *de novo* DSA is due to the reduction of immunosuppression or was caused by the SARS-CoV-2-induced immunological response.

Hence, a SARS-CoV-2 infection that occurs early after kidney transplantation may have a harmful effect on kidney allograft function. Patients undergoing kidney transplantation during the COVID-19 pandemic period should be clearly informed of potential additional risks related to SARS-CoV-2 infection.

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Figure 1

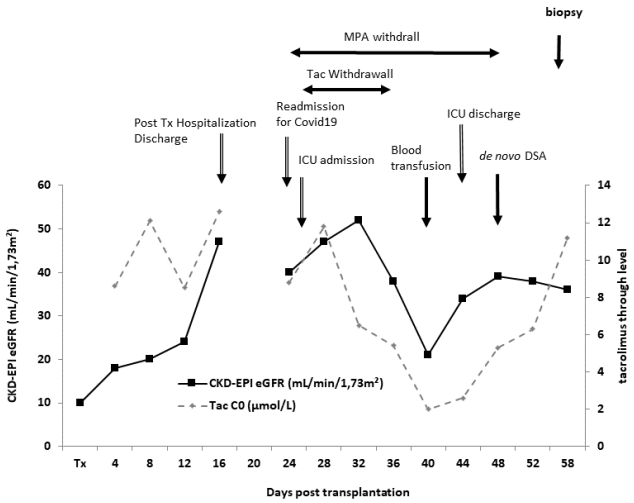
1A Evolution of estimated glomerular filtration rate (eGFR) with the CKD-EPI formula, and tacrolimus trough concentration (C0) according to the time post-transplantation.

Abbreviations: C0, trough concentration; DSA, donor-specific antibodies; ICU, Intensive care unit; MPA, mycophenolic acid; tac, tacrolimus; Tx, transplantation.

1B. Kidney biopsy performed after occurrence of *de novo* DSA (Masson's trichrome, magnification x200).

The biopsy, performed after ICU discharge, found a severe, diffuse proximal tubule injury, in this context suggesting a SARS-CoV-2 kidney injury, associated with an interstitial infiltration (scored Banff i1) and tubulitis (scored Banff t2).

1A



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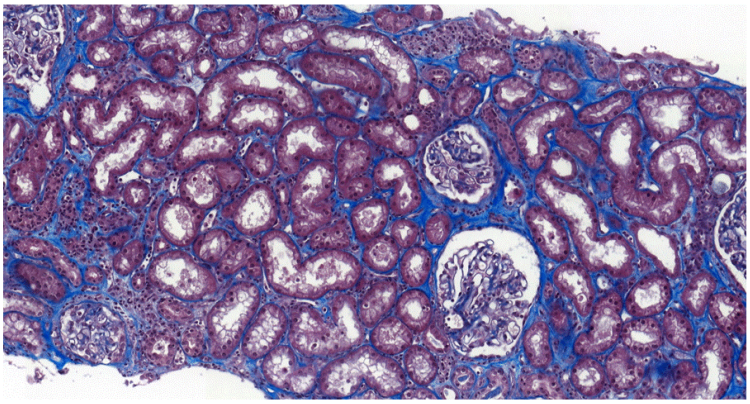
1B



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